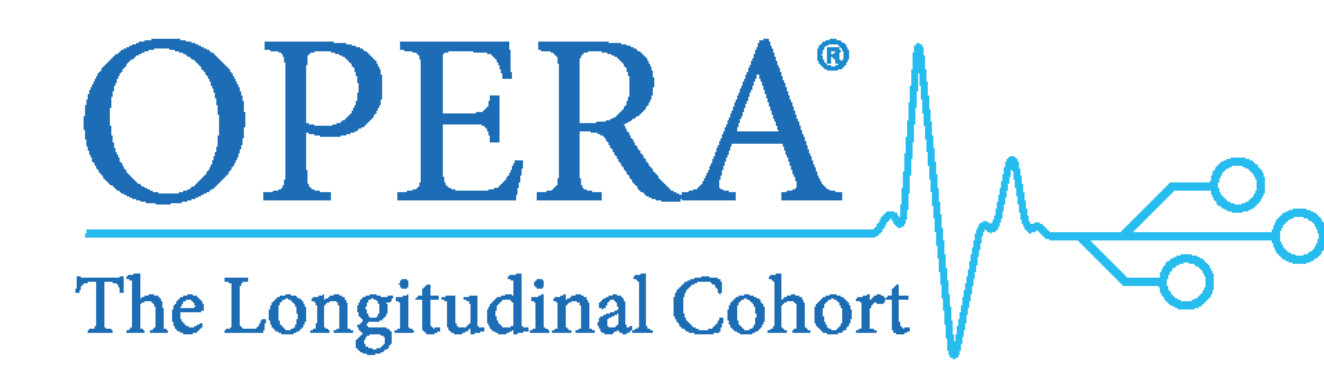


Comparison of a Two-Drug Regimen (Dolutegravir/Rilpivirine) to Standard Three-Drug Regimens in Virologically Suppressed, Treatment Experienced Individuals in the Real World

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Background

- Three antiretrovirals from two classes have long been the standard of care for people living with HIV (PLWH)
- Newer, more powerful antiretrovirals have introduced the potential for effective therapy with fewer agents
- Dolutegravir/rilpivirine (DTG/RPV) was the first single tablet, once daily regimen containing only two antiretrovirals to be approved
- DTG/RPV was approved in the US at the end of 2017

Objective

To compare the effectiveness and durability of DTG/RPV to standard three-drug regimens (3-DR) in a real-world population

Methods

Study population

- **Data source:** OPERA database of electronic health records from 94,852 PLWH (84 clinics, 18 U.S. states/territories) as of 9JAN2019
- **Inclusion Criteria:**
 - HIV- 1 positive, HIV-2 negative, ≥13 years of age
 - Initiated a 2-DR (DTG/RPV) or 3-DR (DTG, EVG, RAL, DRV, RPV, or ATV + 2 NRTIs, boosted or unboosted) between 1JAN2018 and 30JUN2018
 - Last viral load <50 copies/mL on or before initiation of regimen of interest
 - No exposure to DTG/RPV prior to initiation
- **Baseline:** Date of initiation of 2-DR or 3-DR of interest
- **Study outcomes:**
 - Virologic failure: 2 VL ≥ 200 copies/mL or 1 VL ≥ 200 copies/mL + regimen discontinuation
 - Sustained suppression: Last VL <50 copies/mL and <200 copies/mL
 - Treatment discontinuation: Modification or discontinuation of regimen of interest
- **Follow-up until:**
 - Regimen discontinuation
 - Death or
 - Study end (31DEC2018)

Analyses

- Description of patient characteristics and outcomes
 - Categorical variables: Pearson's chi-square or Fisher exact tests
 - Continuous variables: Wilcoxon rank-sum
- Time to discontinuation and virologic failure
 - Kaplan-Meier methods
 - Multivariable Cox Proportional Hazards models

Results

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic n (%)	DTG/RPV (n=259)	3-DR (n=2,792)	p-value
Age ≥50 years	143 (55.2%)	1,093 (39.1%)	<.0001
Female sex	38 (14.7%)	534 (19.1%)	0.2303
African American race	78 (30.1%)	1,131 (40.5%)	0.0011
Hispanic ethnicity	88 (34.0%)	719 (25.8%)	0.0041
Care in Southern US	172 (66.4%)	1,355 (48.5%)	<.0001
Hx of AIDS	68 (26.3%)	777 (27.8%)	0.5880
CD4 Count >500 cells/ μL	205 (79.2%)	1,986 (71.1%)	0.1100
Hx of Syphilis	72 (27.8%)	1,001 (35.9%)	0.0094
Any Comorbidity	224 (86.5%)	2,218 (79.4%)	0.0067

Figure 1. Distribution of Core Agents Among the 3-DR Group

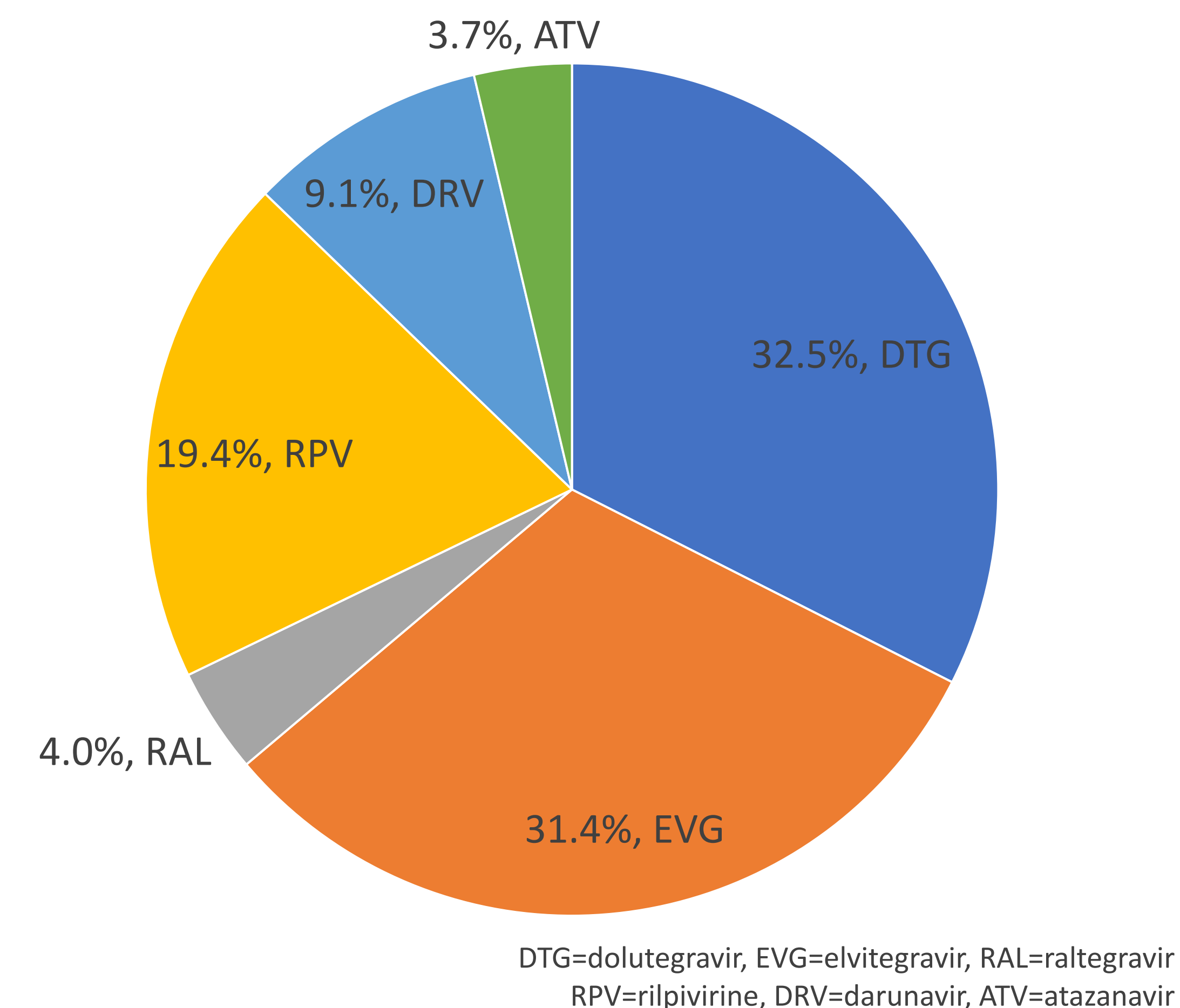


Table 2. Durability and Virologic Suppression with 2-DR versus 3-DR

Outcome (n, % or median, IQR)	DTG/RPV (n=259)	3-DR (n=2,792)	p-value
Durability			
Weeks on regimen	36.4 (29.9 – 43.1)	37.7 (28.3-48.4)	0.0252
Discontinuations	25 (9.7%)	438 (15.7%)	0.0096
Suppression among those tested			
Last VL < 50 copies/mL	209 (92.1%)	2,003 (90.0%)	0.3139
Last VL < 200 copies/mL	222 (97.8%)	2,134 (95.9%)	0.2083

Figure 2. Unadjusted Cumulative Probability of Discontinuation of 2-DR versus 3-DR

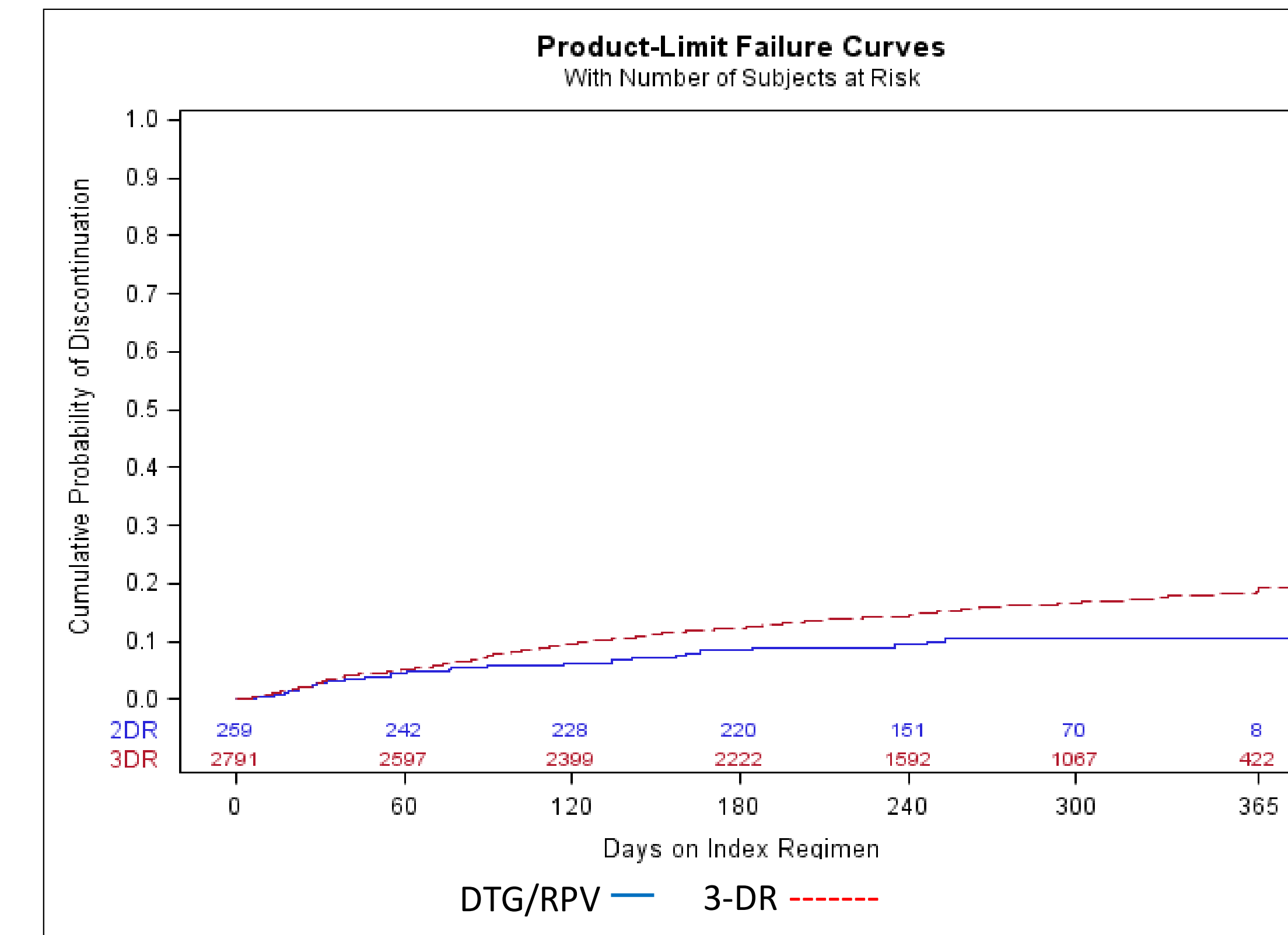


Figure 3. Unadjusted Cumulative Probability of Virologic Failure of 2-DR versus 3-DR

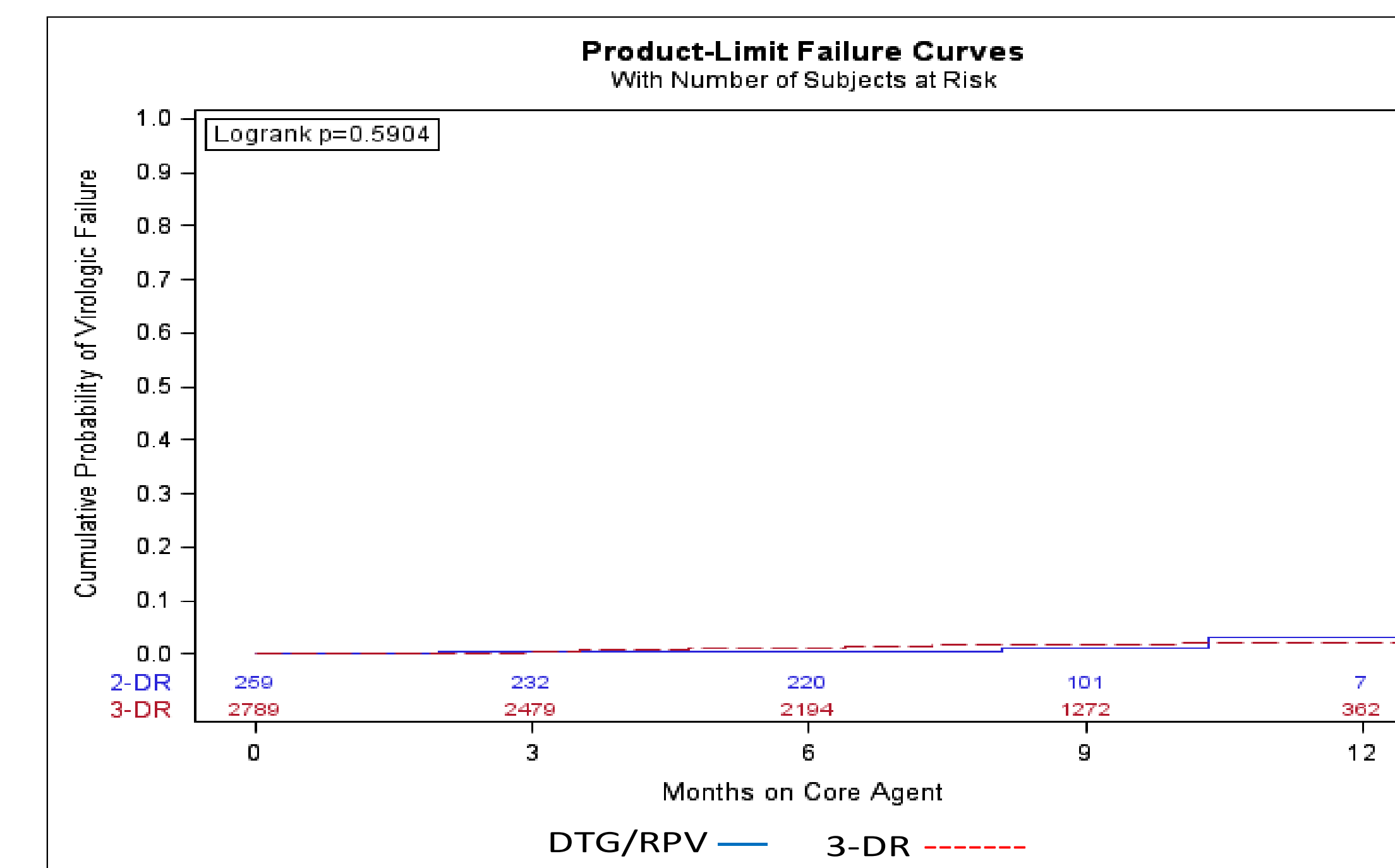


Table 3. Virologic Failure with 2-DR versus 3-DR

	DTG/RPV (n=259)	3-DR (n=2,792)	p-value
Virologic Failure among those tested			
Virologic Failures, n (%)	3 (1.3%)	44 (2.0%)	0.7972
Incidence Rate*	1.7 (0.6, 5.4)	2.3 (1.7, 3.1)	0.6937
Unadjusted HR [^]	1.0	1.38 (0.43, 4.43)	0.8085
Adjusted HR [¯]	1.0	1.16 (0.35, 3.79)	0.8085

*IR=Incidence Rate per 100 person-years (95% CI)
[^]HR=Hazard Ratio (95% CI)

[¯]HR adjusted for age, sex, race, ethnicity, region, CD4 cell count, history of comorbidities

Discussion

- DTG/RPV users differed from 3-DR users notably (Table 1)
 - DTG/RPV users were older, more likely to be Hispanic, to live in the southern US, and have comorbidities
 - 3-DR users were younger, more likely to be African American, and have a history of syphilis (an indicator of a complex lifestyle)
- DTG/RPV users were followed for less time, experienced fewer discontinuations, and did not differ in sustained suppression compared to 3-DR users (Table 2, Figure 2)
- Virologic failure was uncommon early and did not differ between DTG/RPV and 3-DR users (Table 3, Figure 3)
- Strengths: Large, diverse population of PLWH in the US
- Limitations: No reasons for those who discontinued or resistance data for those who failed

Key Findings

Among ART-experienced, virologically suppressed PLWH initiating DTG/RPV or standard 3-DR, there was no observed difference in their ability to remain suppressed or risk of virological failure in a real-world setting over the first 12 months of approval

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